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Treatment of epilepsy in general hospitals: do patients and neurologists agree on success or failure?

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***Objective*:** Opinions of patients and neurologists about aspects of their epilepsy and their treatment were compared.
***Method*:** Thirty-two neurologists, working in general hospitals, included 198 patients aged 16 years or more. Both neurologist and patient independently completed a questionnaire consisting of simple open questions about the epilepsy and the drug treatment. The average characteristics for this group are very similar to characteristics of the general population: age and gender distribution, highest completed educational level, occupational participation and family circumstances are not statistically significant from the general population.
***Results*:** Neurologists and patients appear to agree about most areas that we assessed: seizure count, severity of epilepsy, efficacy and tolerability of the treatment and impact of the epilepsy and treatment on daily life (as expressed in the 'Quality of Life ratings'). Detailed analysis showed that this agreement is partly artificially increased by the group with good outcome and less strong or even absent for the more severe epilepsies. For seizure count, we see 96.4% agreement for the group with low seizure frequency and 73.1% agreement in case of high seizure frequency. For the evaluation of severity of the epilepsy, 73.2% agreement is found for mild classification and 16.6% agreement for the severe classification. Agreement on Quality of Life (QOL) is almost complete in patients with excellent QOL (91% agreement) and almost absent for a low QOL (17% agreement). Finally, the same pattern is found for reports on side-effects of the medication. Both neurologists and patients report side-effects in about 40% of the cases. This suggests excellent agreement but individual data show that agreement is only satisfactory for the milder epilepsies (16.2% vs. 16.2%). For the more severe agreement is almost absent (4.1% of the neurologists vs. 13.4% of the patients).
***Discussion*:** Possibly, it is more difficult for the neurologist to perceive and appraise all relevant factors in the case of complex epilepsies. Alternatively, subjective definitions and assumptions of patients differ from the standards set by the neurologists in the case of continuing seizures.

The clinical relevance of our findings is that, especially in the cases of more severe and refractory epilepsies, patients' opinions are of utmost importance and we cannot take our own opinions and evaluations at face value.

Key words: epilepsy; treatment; AEDs; side-effects; tolerability.

INTRODUCTION

Treatment of epilepsy will be influenced by the complex interactions between the patient and his or her neurologist. Because subjective factors are an essential mediator in this interaction, both parties may have different perspectives and goals: Are suppressing seizures or avoiding side-effects the most important aim of the treatment? Is 1 seizure per month acceptable or not? Is having a seizure affecting 'Quality of Life'? To what extent are side-effects of the treatment acceptable? Such treatment decisions have to be based on subjective information provided by the patient, influenced by the—often implicit—goals set by the patients[1–3]. Gold standards for important treatment criteria, such as occurrence, severity and

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tolerability of side-effects, are seldomly available or—if available—valid[4,5]. Correlation between the 'objective measurements by tests' and the subjective opinion of the patient or his treating physician is generally low in all kind of clinical populations[6–8]. Even counting seizures may seem to be easy, but many studies have questioned the reliability and accuracy of seizure counts even when controlled seizure diaries are used[9].

So far, it is unknown to what extent neurologists and patients agree or disagree about the epilepsy, and about success or failure of treatment. Instead of correlating the opinions of patients with some gold standard, we compared the subjective opinion of patients with the subjective opinion of the neurologists on general aspects of their epilepsy and their treatment. Our study is based on patients with epilepsy treated in general hospitals in The Netherlands.

METHOD

Neurologists in general hospitals were asked to participate in this study. These neurologists were randomly selected from the neurologists working in general hospitals in The Netherlands. They were asked to hand over a questionnaire to each consecutive patient (up to 20 patients) aged 16 years or more with a confirmed diagnosis of epilepsy that visited their outpatient department in the period mid to end 2000. Patients with insufficient knowledge of the Dutch language were excluded. Each neurologist could include a maximum of 20 patients. In total, 32 neurologists accepted to participate and 264 patients received the questionnaires (on average about 8 patients per neurologist) of which 198 were returned (response rate of 76%). The sample size is sufficiently large to allow generalisation of the findings to the total population of patients under the care of neurologists working in general hospitals[10,11]. In addition, the neurologists were also requested to complete a questionnaire about the patients that received a questionnaire. This was done independently of the patients. The questionnaire consisted of simple open questions about the epilepsy and the drug treatment. The Quality of Life (QOL) rating used the Qolie-10[12].

The study was conducted in accordance with the ICH GCP guideline (1997) and approved by an independent ethics committee. Subjects gave written informed consent before entering the study.

RESULTS

To control whether the sample is representative, we compared the demographic characteristics of our sample with the general population:

Table 1: Age distribution of the study population versus the general population.

	% study sample	% general population
16–29 years	14	18
30–49 years	40	32
50–65 years	28	17
>65 years	14	13

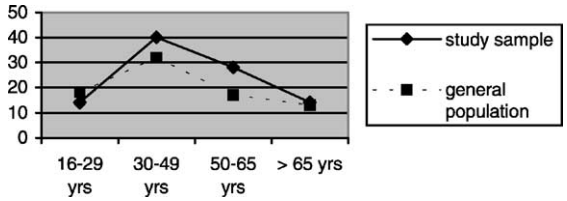

Fig. 1: Age distribution for the study sample and general population.

Mean age of the study population was 46.7 years (SD 16.1). Table 1 shows that the age distribution in our study sample is representative for the general population in The Netherlands[13] (Chi-square = 2.682; df = 3; $P \geq 0.50$).

Fig. 1 illustrates the concurrence of both age distributions:

Gender distribution was 55% male versus 45% female, which is not significantly different from the general population in The Netherlands[13].

Table 2 shows the highest completed educational level of the patients compared to the distribution of highest completed educational level in the general population in The Netherlands[13].

Although there is an overrepresentation of lower educational levels in our study sample, compared to the general population, the difference is not statistically significant (Chi-square = 6.173; df = 4; $P \geq 0.10$). In total, 41.6% of the patients have a full-time employment and 8.5% have paid part-time jobs. This is not statistically significant different from the general population (56% of the Dutch population aged >16 have a paid job of at least 12 hours per week[13]; Chi-square = 0.0009; $P = 0.99$).

The family circumstances of our patients are similar to those in the general population as shown in Table 3 (Chi-square = 0.250; df = 2; $P = 0.98$).

Table 2: Highest completed educational level for patients in our study versus the general population.

	% patients in the study sample	% in the general population
Primary education	10.9	4
Lower vocational training	24.1	22
Lower secondary education	32.6	40
Higher secondary education	7.6	9
Higher education	14.6	25

Table 3: Family circumstances for patients in our study versus the general population.

	% patients in the study sample	% in the general population
No partner/living single	30.9	34
Partner	42.4	39
Partner with children	26.7	27

The majority of the patients in our sample (55.3%) had generalised seizures (either primarily generalised or secondarily generalised), 15% had simple partial seizures and 34.5% complex partial seizures. The average period from seizure onset to the present visit in the hospital is 13 years for the age group until 29 years, 17 years for the age group 30–49 years and 23 years for the age group 50–65 years. For the age group >65 years, the period since epilepsy onset is somewhat smaller (20 years), due to the relative large group with an epilepsy onset at later age. The majority of these patients (77.6%) visit the neurologists at least once or twice per year; the remainder group (22.4%) only come to the hospital in case of problems. Most patients use monotherapy of antiepileptic drugs (AEDs) (68.3%), 29.6% have polytherapy and four patients do not use any medication (but still visit the outpatient department of the hospital). Valproate is the most frequent used AED and is used in 40% of the patients; carbamazepine is used in 28.4% of the patients (combined with oxcarbazepine this is 36.7%), phenytoin in 9.1% of the patients and phenobarbital in 5.3% of the patients. The newer AEDs are only used in small percentages of the patient group (<2%). Most patients are on unchanged treatment during the last 12 months (74.4%). Almost all patients report satisfactory compliance.

Comparison between the patients and neurologists reports

Seizure frequency

Agreement between the patients and neurologists for the number of seizures that occurred during the last year was excellent (Table 4).

Table 4: Number of seizures during the last year according to patients and neurologists.

	% according to patient opinion	% according to neurologist opinion
Seizure free >1 year	55.8	57.9
1–3 seizures per year	23.2	25.4
4–11 seizures per year	12.0	9.9
12–20 seizures per year	4.4	4.3
>20 seizures per year	4.6	2.5

Table 5: Results for ranking of severity of epilepsy for patients versus neurologists.

	Severity according to patient	Severity according to neurologist
% score: 1, 2 (mild)	58.4%	62.7%
% score: 3–5 (average)	33.3%	28.8%
% score: 6, 7 (severe)	4.4%	4.8%
Average rank (range 1–7)	2.58 (1.89)	2.59 (1.76)
Missing	3.9%	3.7%

Spearman's Rho shows a statistically significant correlation for the comparison between the patients and neurologists as a group (correlation = 0.83; $P \leq 0.001$). Looking at the agreement per individual, the percentage agreement is highest for the patients who are seizure free (96.4% agreement between the patients and neurologists for the patients who are seizure free for >1 year) and lower for the other (smaller) categories. For the patients with high seizure frequency (>12 seizures per year), the percentage agreement is 73.1%.

Severity of the epilepsy

A subjective impression for the severity of the epilepsy was scored independently by the patients and the neurologists on a scale ranging from 1 = mild to 7 = severe (Table 5).

Agreement between the neurologists and the patients as a group for subjectively rated severity of the epilepsy is good, although there is less agreement than for seizure count (non-parametric Spearman's Rho = 0.28; $P \leq 0.001$). The agreement per individual patient is not as strong as for the seizure frequency and artificially high due to the agreement for the large groups that have a 'mild' classification (73.2% agreement between the neurologists and patients). Agreement for the 'severe' classification is lower (16.6%).

Additional complaints

In total, 70% of the patients have additional complaints besides the seizures. Most frequent complaints are the related areas of fatigue, somnolence, attentional problems ('feeling less alert'). Memory is also a frequent problem (about one third of the patients). For most areas the patients indicate that they are not able to relate this to a cause. Gum problems, weight gain and somnolence are associated with the AED treatment. Speech problems are predominantly seen as an effect of the epilepsy. Table 6 summarises these problems.

If we isolate the percentage of patient complaints that they see as an adverse effect of the antiepileptic treatment and compare this to the percentage of side-effects reported by the neurologists, the respective

Table 6: Complaints mentioned by the patients as well as the probable cause (patient report).

	Total (%)	Seen by the patients as caused by		
		Side-effect AED	Epilepsy	Unknown cause
Fatigue	36	25	22	**53**
Attentional problems	34	27	21	**52**
Somnolence	33	**51**	13	36
Memory problems	33	19	26	**56**
Headache	29	7	28	**66**
Tremor	27	30	30	40
Slowing	23	27	25	48
Weight gain	19	**58**	0	42
Dizziness	19	15	49	36
Gum problems	15	**50**	0	**50**
Speech difficulties	14	7	**55**	38
Walking difficulties	13	11	36	**54**
Decreased possibilities	12	15	31	**54**
Visual problems	11	25	29	46
Aggression	11	13	13	**74**
Depression	10	10	19	**71**
No complaints	30			

Items representing >50% of the patients in bold.

Table 7: Quality of Life (QOL) as reported by the patient versus neurologist opinion.

	QOL as reported by the patient	QOL of the patient as observed by the neurologist
% high QOL (score: 1, 2)	79.0%	85.5%
% average QOL (score: 3)	14.9%	10.2%
% low QOL (score: 4, 5)	6.1%	4.3%
Average score (1–5), 1 = excellent; 5 = worst possible	2.01 (0.8)	1.78 (0.8)

Table 8: Percentage agreement on Quality of Life (QOL) estimation by neurologist and patient.

Patient	Neurologist			
	Excellent	Average	Worst possible	Total (*N*)
Excellent	$n = 139$ (91%)	$n = 10$	$n = 4$	153
Average	$n = 17$	$n = 9$ (31%)	$n = 3$	29
Worst possible	$n = 9$	$n = 1$	$n = 2$ (17%)	12
Total (*N*)	165	20	9	194

percentages (41.7% for the patients and 42.6% for the neurologists) show a statistically significant correlation (Rho = 0.57; $P \leq 0.001$). Neurologists and patients as a group therefore agree on the occurrence of side-effects. Again, there is statistically significant disagreement in the severe types of epilepsy (where more patients use polytherapy): 4.1% of the neurologists report side-effects in their patients whereas 13.4% of the patients report side-effects (Chi-square = 13.752; df = 1; $P \leq 0.001$).

Quality of Life

The average rating of QOL (ranging from 1 = excellent to 5 = worst possible) is excellent for the majority of the patients (2.01: patient report). The correlation between the patients and neurologists as a group is statistically significant (Rho = 0.45; $P \leq 0.001$) with a somewhat more positive evaluation of QOL by the neurologists, compared to the patients (Table 7).

The agreement per individual patient (Table 8), however, shows that the agreement is largest for 'excellent' QOL (91% agreement), and almost absent in case of low QOL (17%).

DISCUSSION

We studied a sample of 198 patients with epilepsy treated in general hospitals. The average characteristics for this group are very similar to characteristics of the general population: age and gender distribution, highest completed educational level, occupational

participation and family circumstances are not statistically significant different from the general population. There is a trend—even in this group with uncomplicated epilepsy—for a somewhat lower achieved educational level.

The majority of the patients are seizure free (57.9%) and another one fourth of the sample have only a few seizures per year; 83.3% of this group may therefore be considered well controlled. This is in line with the results of epidemiological studies in the group of patients with uncomplicated epilepsy[14]. About 70% of the patients in our study use monotherapy and are mostly treated with valproate (40% of the patients) or carbamazepine (29% of the patients, combined with oxcarbazepine this is 36.7%). Remarkably, only small percentages of the patients use the newer AEDs (all $<2\%$).

Neurologists and patients as a group appear to agree about most areas that we assessed: seizure count, severity of epilepsy, efficacy and tolerability of the treatment and impact of the epilepsy and treatment on daily life (as expressed in the 'Quality of Life ratings'). This is reassuring for clinical practice, given the dependency of treatment choices on agreement about success and failure of treatment. Nonetheless, some additional comments have to be made. The excellent agreement may be caused by the fact that most patients were treated for a considerable period of time and the results would then represent the result of the communication between the neurologists and their patients over time. Nonetheless, if we inspect the individual comparisons between each patient and his or her treating neurologist, then the agreement appears only high for those patients with mild epilepsy and good outcome, whereas this agreement is less strong or even absent for the more severe epilepsies. For seizure count, we see 96.4% agreement for the patients with low seizure frequency and 73.1% agreement in case of high seizure frequency; for severity of the epilepsy, 73.2% agreement is found for mild classification and 16.6% agreement for the severe classification. This is probably an effect of differences in the 'subjective definition' of severity between the neurologists and patients. It is conceivable that both 'parties' have different criteria and assumptions here. The same lack of agreement is seen for the evaluation of the overall psychosocial situation of the patients, expressed in 'Quality of Life estimates'. Neurologists seem to be able to estimate the subjective 'Quality of Life' of the patients as a group. This agreement is, however—as for the other areas—artificially increased in our study by the excellent treatment results in this specific patient population with almost 60% of the patients being seizure free. Earlier studies showed a high correlation between the seizure control and QOL and the major factor contributing to QOL in patients with epilepsy was seizure frequency, specifically whether patients are seizure free or not[15]. Our study in patients with uncomplicated epilepsy does not rule out the possibility that the agreement between the patients and neurologists is much lower in refractory epilepsy. Agreement on QOL is almost complete in patients with excellent QOL (91% agreement) but almost absent for patients with a low QOL (17% agreement). Finally, the same pattern is found for reports on side-effects of the medication. Both neurologists and patients report side-effects in about 40% of the cases. This suggests excellent agreement, but individual data show that agreement is only satisfactory for the milder epilepsies (16.2% vs. 16.2%). For the more severe epilepsies (were most patients use polytherapy), agreement is almost absent, with 4.1% of the neurologists and 13.4% of the patients reporting side-effects. This disagreement between the neurologists and patients in cases of more severe epilepsies may be partly due to differences in 'subjective definition' of severity (we asked for a subjective rating of severity), although the consistency of the discrepancy (occurring not only in the case of high severity ranking, but also in high seizure frequency and low QOL scores) points to the fact that differences in subjective perspectives and goals of treatment have a greater impact in more complicated epilepsies and treatments.

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